

ANDA 75-049

August 2, 2001

Geneva Pharmaceuticals, Inc.
Attention: Beth Brannan
2555 W. Midway Blvd.
Broomfield, CO 80038-0446

Dear Madam:

This is in reference to your abbreviated new drug application dated December 31, 1996, submitted pursuant to Section 505(j) of the Federal Food, Drug, and Cosmetic Act (Act), for Fluoxetine Capsules USP, 10 mg and 20 mg.

Reference is also made to the Tentative Approval letters issued on June 15, 1999 and April 30, 2001 and to your amendments dated September 5, 1997; January 5, May 18, June 6, and July 31, 2001.

The listed drug product referenced in your application is subject to a period of pediatric exclusivity that expires on August 2, 2001. In addition, the listed drug product is subject to a period of patent protection which expires June 2, 2004, (U.S. Patent No. 4,626,549 [the '549 patent]). Your application contains a Paragraph IV Certification and a Method of Use Statement under Section 505(j)(2)(A)(vii)(IV) and Section 505(j)(2)(A)(viii) of the Act to the '549 patent. You informed us that Eli Lilly and Company initiated a patent infringement action against you on your Paragraph IV Certification on the challenged claim in United States District Court for the Southern District of Indiana (Eli Lilly and Company v. Barr Laboratories, Inc., Apotex Inc., Interpharm Inc., Bernard C. Sherman, and Geneva Pharmaceuticals, Inc., Civil Action No. IP 96-0491 C B/S). You have also notified us that you prevailed on one claim in both the district court and in the court of appeals and made a Method of Use Statement to another claim.

We have completed the review of this abbreviated application and have concluded that the drug is safe and effective for use as recommended in the submitted labeling. However, because of the unique (split) 180-day generic drug exclusivity issues associated with this drug product, the

Agency is prohibited from approving both strengths at this time. **Thus, only the 10 mg strength of the drug product is approved at this time. The 20 mg strength shall remain tentatively approved** and will not receive final approval until the remaining 180 days of exclusivity has expired. The Division of Bioequivalence has determined your Fluoxetine Capsules USP, 10 mg to be bioequivalent and, therefore, therapeutically equivalent to the listed drug (Prozac Capsules, 10 mg of Eli Lilly and Company). Your dissolution testing should be incorporated into the stability and quality control program using the same method proposed in your application.

With respect to 180-day generic drug exclusivity and its impact on the approvability of the various strengths presented in this application, we note that Geneva Pharmaceuticals, Inc. (Geneva) was the first to submit a substantially complete ANDA with a Paragraph IV Certification for the 10 mg strength only. Therefore, Geneva is eligible for 180-days of market exclusivity for the 10 mg strength. Subsequent applications for the 10 mg strength will be eligible for final approval not earlier than one hundred eighty days after:

the date the Secretary receives notice from the applicant under the previous application of the first commercial marketing, or

the date of a decision of a court in action described in clause (ii) holding the patent which is the subject of the certification to be invalid or not infringed, whichever is earlier [Section 505(j)(B)(iv)].

With respect to the "first commercial marketing" trigger for the commencement of exclusivity, please refer to 21 CFR 314.107(c)(4). The Agency expects that you will begin commercial marketing of the 10 mg strength of this drug product in a prompt manner. Please submit correspondence to your application stating the date you commence commercial marketing of the 10 mg strength, or the date of a decision of the court holding the relevant patent invalid, unenforceable or not infringed.

If you have any questions concerning the effective date of approval of an abbreviated new drug application and the Agency's elimination of the requirement that an ANDA applicant successfully defend a patent infringement suit to be eligible for 180-days of marketing exclusivity, please

refer to the interim rule published in the November 5, 1998 Federal Register (Volume 63, No. 214, 59710).

We are unable to grant final approval to the 20 mg strength at this time because an abbreviated application for Fluoxetine Capsules USP, 20 mg containing a Paragraph IV Certification for this strength was accepted for filing by OGD prior to the filing of your application. Subsequent applications for the 20 mg strength may not be approved earlier than one hundred and eighty days after:

the date the Secretary receives notice from the applicant under the previous application of first commercial marketing, or

(2) the date of a decision of a court in action described in clause (ii) holding the patent which is the subject of the certification to be invalid or not infringed, whichever is earlier [Section 505(j)(B)(iv)].

Under Section 506A of the Act, certain changes in the conditions described in this abbreviated application for the 10 mg strength require an approved supplemental application before the change may be made.

Post-marketing reporting requirements for this abbreviated application for the 10 mg strength are set forth in 21 CFR 314.80-81 and 314.98. The Office of Generic Drugs should be advised of any change in the marketing status of the 10 mg strength Fluoxetine Capsules USP.

We request that you submit, in duplicate, any proposed advertising or promotional copy, which you intend to use in your initial advertising or promotional campaigns. Please submit all proposed materials in draft or mock-up form, not final print. Submit both copies together with a copy of the proposed or final printed labeling to the Division of Drug Marketing, Advertising, and Communications (HFD-40). Please do not use Form FD-2253 (Transmittal of Advertisements and Promotional Labeling for Drugs for Human Use) for this initial submission.

We call your attention to 21 CFR 314.81(b)(3) which requires that materials for any subsequent advertising or promotional campaign be submitted to our Division of Drug Marketing, Advertising, and Communications (HFD-40) with a completed Form FD-2253 at the time of their initial use.

With respect to the continuation of the tentative approval status of the 20 mg strength of this drug product, our decision is based upon information available to the Agency at this time (i.e., information in your application and the status of current good manufacturing practices (CGMPs) of the facilities used in the manufacture and testing of the drug product), and is subject to change on the basis of new information that may come to our attention.

To provide for final approval of the 20 mg strength, please submit a supplemental application as directed below. The Agency will provide written notice of the information needed to determine the earliest possible final approval date of your supplemental application for the 20 mg strength under section 505(j)(5)(B)(iv) as soon as such information becomes available. The supplemental application, which must be submitted for prior approval between 60 and 90 days prior to the date you believe this strength will be eligible for final approval, should include updated information such as final-printed labeling, and chemistry, manufacturing and controls data as appropriate. Alternatively, a prior approval supplement should be submitted to request final approval of this strength and stating that no changes have been made to the application since the date of this letter. Because of the unique circumstances associated with exclusivity for this drug product, the office will entertain your request that the supplemental application be granted "expedited review" status.

Any changes in the conditions outlined in this abbreviated application and the status of the manufacturing and testing facilities' compliance with current good manufacturing procedures are subject to Agency review before final approval of the supplemental application will be made.

In addition to, or instead of the supplemental application requesting final approval of the additional strength, the Agency may at any time prior to final approval, request that you submit an informational document containing the information stated above.

Failure to submit the supplemental application or informational document may result in rescission of the tentative approval determination, or delay in issuance of the final approval letter for the 20 mg strength.

The 20 mg strength of Fluoxetine Capsules USP may not be marketed without final Agency approval under section 505 of the Act. The introduction or delivery for introduction into interstate commerce of these unapproved strengths before the final approval date is prohibited under section 501 of the Act. Also, until the Agency issues the final approval letter, the 20 mg strength of the drug product will not be listed in the Agency's "Approved Drug Products with Therapeutic Equivalence Evaluations" list (the "Orange Book").

Should you have any questions about the approval status of the various strengths of drug product presented in your application, or about the timing or content of the supplemental application to provide for final approval of the remaining strength, please contact Mr. Jeen Min, Project Manager, at (301) 827-5849.

Sincerely yours,

Gary Buehler
Director
Office of Generic Drugs
Center for Drug Evaluation and Research